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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/528,000	03/21/2005	Noriyuki Kizaki	Q86432	7567

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EXAMINER	
MEAH, MOHAMMAD Y	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 02/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/528,000	KIZAKI ET AL.	
	Examiner	Art Unit	
	Mohammad Meah	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *5-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/17/05, 3/21/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant, on date 12/14/2005 elected without traverse Group I (claims 1-4) for examination.

Election/Restriction

Applicant, on date 12/14/2005 elected without traverse Group I (claims 1-4), drawn to a polypeptide that stereoselecively reduce N-benzyl-3-pyrrolidinone for examination. Groups II-III (claims 5-23) of election/restriction-office action of date 11/21/2005 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected Groups.

Priority

Acknowledgement is made of applicant's priority date based on application filing date of 09/19/2003 in Japan: Application No. pct/JPO 3/11957 and filing date 09/19/2002 in Japan: Application No. Japan 2002-272976.

Claim Rejections

35 U.S.C 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement

thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The claimed inventions 1-4 are rejected under 35 USC 101 because the claimed invention directed to non-statutory subject matter.

In the absence of the hand of man, naturally occurring genes are non-statutory subject matter (Diamond v. Chakrabarty, 206 USPQ 193 (1980). The polypeptide in claims 1-4 is natural substance. The rejection may be overcome by amending claims 1-4 to recite wording such as an isolated polypeptide.

35 U.S.C 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2-3 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 2-3 are rejected as the recitation of "derived from" is vague and confusing and make the claims indefinite. Is "derived from" synonymous with "isolated from" or does it more broadly encompass mutants of natural proteins from these organisms? For purpose of further examination it is presumed to mean isolated from.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1 and 2 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 is directed to a genus of carbonyl reductases with a subunit molecular weight of about 28 kD and a mwt of about 55kD for the homo- or heterodimer. Claim 2 encompasses any carbonyl reductases capable of reducing carbonyl compound. As discussed in the written description guidelines the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial

variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. The specification teaches the isolation and characterization of only a single species of such Carbonyl reductase, i.e., that from Devosia riboflavina IFO 13584 having SEQ ID NO: 1. Moreover, the specification fails to describe any other representative species by sufficient identifying characteristics or properties to show that applicant was in possession of the claimed genus.

The identifying characteristics recited in Claim 1, i.e., enzymatic activity, approximate molecular weight of Carbonyl reductase, optimum enzyme activity at pH 5.5-6.0 and temperature 50-55 ^{0}C do not include sufficient characteristics to limit the claimed genus to proteins which are not highly variable in structure. The claim includes a genus of polypeptides having no structural limitations from any source. Therefore carbonyl reductase of claim 1 is so broad as to encompass many carbonyl reductase polypeptides comprising different amino acid sequences (i,e, different structures, for example via varying rearrangements of same number and same type of amino acid residues) as long as they have approximate molecular weight of about 28 kD and a mwt of about 55kD for the homo- or heterodimer, optimum enzyme activity at pH 5.5-6.0 and temperature 50-55 ^{0}C. The specification teaches the structure of only a single representative species of such carbonyl reductase (SEQ ID NO: I). The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of carbonyl reductases with variable structures broadly encompassed by the claim. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the

functionality of carbonyl reductase activity. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Finally it is noted that claim 2 is even broader in scope than Claim 1 and thus clearly fails to provide a sufficient description as discussed above. Thus for all the reasons discussed, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claims 1-2 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the carbonyl reductase of SEQ ID NO: 1 does not reasonably provide enablement for any carbonyl reductase variant comprising polypeptide with any number of substitution, deletion and addition of amino acid residues of the sequence of SEQ ID NO: 1 or any carbonyl reductase with the characteristics recited in claim 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Claim 2 are so broad as to encompass any carbonyl reductase and variant thereof, while claim 1 is so broad as to recite any carbonyl reductase with an optimum pH of 5.5-6,an optimum temperature of 50-55 ^{0}C and a dimeric structure of subunit of

about 28000 mwt each. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of carbonyl reductase broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the amino acid sequence of only one carbonyl reductase.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass any polypeptide having carbonyl reductase activity on any carbonyl reductase having the specific characteristics recited in claim 1 because the specification does **not** establish: (A) regions of the protein structure which may be modified and still

retain carbonyl reductase activity; (B) the general tolerance of carbonyl reductase to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any carbonyl reductase residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any carbonyl reductase. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of carbonyl reductase activity, having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir,1988).

Applicants' isolated polypeptide comprising the amino acid sequence of SEQ ID NO: 1 appears to be novel. Therefore claims limited to isolated polypeptide comprising the amino acid sequence of SEQ ID NO: 1 would be allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mohammad Meah whose telephone number is 571-272-1261. The examiner can normally be reached on 8:30-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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